

Appl. No.: 09/837,235  
Amtd. dated May 28, 2004  
Reply to Final Office Action dated Mar. 31, 2004  
Page 8 of 26

Docket No. 289550-122 US2

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing and Status of Claims:**

Claims 1-9. (Canceled)

Claim 10. (Currently Amended): An isolated protein comprising at least one di-tyrosine cross-link, wherein at least one tyrosine of a di-tyrosine cross-link originates from a point mutation to tyrosine, and wherein the di-tyrosine cross-linked protein retains at least one function displayed by the protein in the absence of di-tyrosine cross-linking.

Claim 11. (Previously Presented): The protein of claim 10, further comprising at least one amino acid which originates from a point mutation from tyrosine such that the amino acid is not cross-linked under cross-linking conditions.

Claim 12. (Previously Presented): The protein of claim 10, wherein the function retained comprises catalytic activity or binding specificity.

Claim 13. (Currently Amended): The protein of claim 10, wherein the protein ~~comprises~~ is an enzyme, an antibody, or a fragment thereof.

Claims 14-17. (Canceled)

Appl. No.: 09/837,235

Docket No. 289550-122 US2

Amdt. dated May 28, 2004

Reply to Final Office Action dated Mar. 31, 2004

Page 9 of 26

Claim 18. (Currently Amended): A method for making a stabilized protein comprising:

(a) selecting one or more residue pairs in a polypeptide chain or chains for di-tyrosine cross-linking, wherein at least one of the selected residues is tyrosine and

(b) mutating at least one of the selected residues to tyrosine; and

(b) (c) cross-linking the residue pairs, pairs;

wherein the di-tyrosine cross-linked protein retains at least one function

displayed by the protein in the absence of di-tyrosine cross-linking, and

wherein at least one tyrosine of a di-tyrosine cross-link originates from a point mutation to tyrosine.

Claim 19. (Currently Amended): The method of claim 18, wherein the di-tyrosine cross-link reaction occurs in the presence of one or more oxidants selected from the group consisting of hydrogen peroxide, oxone, magnesium monoperoxyphthalic acid hexahydrate (MMPP), a photogenerated oxidant, ammonium persulfate, or any combination thereof.

Claim 20. (Currently Amended): The method of claim 19, wherein the di-tyrosine cross-linking is catalyzed by a catalyst selected from the group consisting of polyhistidine, Gly-Gly-His, a metalloporphyrin, a peroxidase or any combination thereof.

Claim 21. (Canceled)

Claim 22. (Currently Amended): The protein of claim 10, wherein the protein comprises is a hormone, a receptor, a growth factor, an enzyme or an antibody.

Appl. No.: 09/837,235

Docket No. 289550-122 US2

Amdt. dated May 28, 2004

Reply to Final Office Action dated Mar. 31, 2004

Page 10 of 26

Claim 23. (Currently Amended): The protein of any of claims 10-13 or 22, wherein the protein further comprises is part of a pharmaceutical composition.

Claim 24. (Previously Presented): The protein of claim 23, wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier.

Claim 25. (Previously Presented): The protein of claim 23, wherein the pharmaceutical composition is suitable for *in vivo* use in humans.

Claim 26. (Currently Amended): The protein of any of claims 10-13 or 22 10-13, 22 or 27, wherein the protein is part of a kit.

Claim 27. (New): The protein of claim 10, wherein the protein is a chimeric polypeptide comprising a hormone, a receptor, a growth factor, an enzyme or an antibody.

Claim 28. (New): A composition comprising a protein of any of claims 10-13, 22 or 27.

Claim 29. (New): The composition of claim 28, wherein the composition is part of a kit.

Claim 30. (New): An isolated stabilized protein obtained from a method comprising:

- (a) selecting one or more residue pairs in a protein for di-tyrosine cross-linking;
- (b) mutating at least one of the selected residues to tyrosine;
- (c) isolating the protein; and

Appl. No.: 09/837,235

Amdt. dated May 28, 2004

Reply to Final Office Action dated Mar. 31, 2004

Page 11 of 26

Docket No. 289550-122 US2

(d) cross-linking tyrosine residue pairs;

wherein the di-tyrosine cross-linked protein retains at least one function displayed by the protein in the absence of di-tyrosine cross-linking, and

wherein at least one tyrosine of a di-tyrosine cross-link originates from a point mutation to tyrosine.

**Claim 31. (New):** The protein of claim 30, further comprising at least one amino acid which originates from a point mutation from tyrosine such that the amino acid is not cross-linked under cross-linking conditions.

**Claim 32. (New):** The protein of claim 30, wherein the function retained comprises catalytic activity or binding specificity.

**Claim 33. (New):** The protein of claim 30, wherein the protein is an enzyme, a hormone, a growth factor, a receptor, an antibody, or a fragment thereof.

**Claim 34. (New):** The protein of claim 30, wherein the di-tyrosine cross-link reaction occurs in the presence of one or more oxidants selected from the group consisting of hydrogen peroxide, oxone, magnesium monoperoxyphthalic acid hexahydrate (MMPP), a photogenerated oxidant, ammonium persulfate, or any combination thereof.

**Claim 35. (New):** The protein of claim 30, wherein the di-tyrosine cross-linking is catalyzed by a catalyst selected from the group consisting of polyhistidine, Gly-Gly-His, a metalloporphyrin, a peroxidase or any combination thereof.

Appl. No.: 09/837,235

Amdt dated May 28, 2004

Reply to Final Office Action dated Mar. 31, 2004

Page 12 of 26

Docket No. 289550-122 US2

**Claim 36. (New):** The protein of claim 30, wherein the protein is a chimeric polypeptide comprising a hormone, a receptor, a growth factor, an enzyme or an antibody.

**Claim 37. (New):** A composition comprising a protein of claim 30 or 36.

**Claim 38. (New):** A kit comprising the protein of claim 30 or 36.

**Claim 39. (New):** A kit comprising the composition of claim 37.